REMARKS

Claims 16-21, 28-31 and 38-44 are pending in this application. Claims 16, 21, 39, 40 and 41 are amended herein to advance the lengthy prosecution of this application to closure. Support for these amendments is found in the language of the original claims and throughout the specification, as set forth below. It is believed that no new matter is added by these amendments.

Claims 38, 42 and 44 are canceled herein without prejudice to the filing of a continuation application for further prosecution. In particular, cancellation and/or amendment of the present and previously pending claims is not be interpreted as acquiescence to or agreement with previous rejections in the prosecution of claims in subsequent applications, as applicants do not agree with the rejection of the claims as presented in the Amendment of January 6, 2004 as introducing new matter and maintain that the new matter rejection is legally improper and without basis.

In light of the amendments presented herein and the following remarks, applicants respectfully request reconsideration of the pending application, entry of these amendments and allowance of the pending claims to issue.

I. Use of the phrase "consisting essentially of" in the amended claims

Applicants direct the Examiner's attention to MPEP § 2111.03, wherein the phrase "consisting essentially of" is described as meaning that the scope of the claim is limited to the specified materials and "those that do not materially affect the basic and novel characteristics of the claimed invention." In the context of the second liquid of the methods of this invention, this phrase is to be interpreted to mean that the liquid can include materials of this invention that do not affect the functional capabilities of the

liquid to facilitate binding of single strand nucleic acid to solid phase. Such materials (e.g., Tris-HCl; Triton X-100; NaOH; H_2O) are described in the specification on page 7, lines 19-32). Thus, applicants request that the Examiner interpret this phrase as provided in the claims as amended herein accordingly.

II. Rejection under 35 U.S.C. § 102(b)

The Office Action states that claims 16-21, 28-31 and 38-44 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Bastian et al. Specifically, the Office Action states that Bastian et al. discloses a method of separating nucleic acid mixtures into their double stranded and single stranded fraction and that all nucleic acids are simultaneously adsorbed in a mineral substrate, then separated by fractional elution into double stranded and single stranded nucleic acids, or double stranded and single stranded nucleic acids of a sample are selectively adsorbed in a mineral substrate. The Office Action further states that Bastian et al. teaches that the double stranded nucleic acid predominantly binds to the first mineral support and after optionally performed washings steps, can be eluted under conditions of low ionic strength or with water and that the non-adsorbed single-stranded nucleic acids collected are subsequently adjusted and can be adsorbed to a second mineral support and become eluted under conditions of low ionic strength or with water. The Office Action goes on to describe the teachings of Bastian et al. as including a treatment condition containing a chaotropic substance and a mineral support consisting of porous or non-porous metal oxides, silica gel or glass and a particle size of 0.1 μm to 1000 μm. The Office Action also states that Bastian et al. teaches that for binding double stranded nucleic acid to mineral supports, the solution contains guanidinium thiocyanate with a concentration of 1 to 8 M and EDTA with a concentration of from 5 mM to 200 mM and that magnesium chloride in a concentration of from 0.1 to 10 M may also be used in combination for lysing or binding the sources containing nucleic acids and that the complexes comprise alkaline earth metal ions bound to EDTA. From these teachings,

the Examiner concludes that claims 16-21, 28-31 and 38-44 are anticipated by Bastian et al.

The Bastian et al. reference does not anticipate the claimed invention. Specifically, applicants point out that the invention set forth in the Bastian et al. patent and PCT publication is based on the discovery by Bastian et al. that variations in the concentration of materials containing alcohol groups in a binding solution allowed for the differential binding of single stranded nucleic acid or double stranded nucleic acid to a solid support. That this is the discovery of the Bastian et al. invention is set forth in the U.S. patent in column 4, lines 17-43, wherein it is stated:

> FIG. 1 shows the binding of single-stranded/double-stranded nucleic acid exemplified by single-stranded RNA and double-stranded DNA. Described here is the RNA/DNA binding from a tissue lysate to a mineral support as a function of the concentration of a material containing alcohol groups (here, ethanol) and a chaotropic substance (here, GTC). Under the condition that the concentration of one of the substances, alcohol or chaotropic substance, is constant, it is found that at a high alcohol concentration and/or amount of chaotropic substance, both types of nucleic acid (RNA/DNA) are bound to the mineral support. If the concentration of one or both substances (alcohol or chaotropic substance) becomes less than a defined value, none of the nucleic acids will bind to the mineral support to any substantial extent. Surprisingly, in between, RNA and DNA will bind to the mineral support to such different extents as can be made use of for the separation of the nucleic acids. Thus, proceeding from cells, and after lysis of the cells with a high concentration of chaotropic substances, the concentrations of chaotropic substance and material containing alcohol groups can be adjusted by subsequent addition of a material containing alcohol groups or a mixture of material containing alcohol groups and water or buffer such that a selective binding of the RNA is achieved while the DNA remains in the breakthrough. In the example according to FIG. 1, concentrations of 1.75 M GTC and 30% by volume of ethanol would be selected in order to achieve a

separation of RNA from DNA by fractional binding.
(Emphasis added.)

Thus, the teachings of the Bastian et al. patent are clearly directed to methods of separating single stranded nucleic acid from double stranded nucleic acid by altering the concentration of alcohol in the solution for binding single stranded nucleic acid. Thus, it is clear that the presence of alcohol in the reagents taught by Bastian et al. materially affects the basic characteristics of the methods taught therein. This is reflected in every example recited in the Bastian et al. specification, wherein all enabling descriptions of a method of separating single and double stranded nucleic acids include reagents comprising material containing alcohol groups.

Specifically, in column 9, line 61 through column 13, line 53 of the Bastian et al. patent, 13 examples are provided. In each example, the single stranded nucleic acid is bound to the solid support by contacting the single stranded nucleic acid with a binding reagent containing alcohol. Specifically, in example 1, a range of alcohol concentrations from 10% to 50% is applied in a binding reagent to a cell lysate while maintaining a constant GTC concentration. It is stated in the Bastian et al. specification in column 10, lines 21-25 that "...the RNA fraction will bind to the mineral support under the conditions described already from ethanol concentrations of greater than 25% whereas the DNA fraction will bind only from ethanol concentrations of greater than 40%."

The Bastian et al. specification further states that in examples 2-8, the alcohol/salt mixtures were selected for the selective binding of single stranded nucleic acid. (column 10, lines 28-30) In particular, in example 2, single stranded nucleic acid was contacted with binding reagent B4 (70% ethanol in water); in example 3, single stranded nucleic acid was contacted with an ethanol-containing lysis buffer, L5 (2.5 M GTC, 25 mM Na citrate, pH 7.5, 1% β-MSH, 30% ethanol) which served as the binding reagent; in example 4, single stranded nucleic acid was contacted with the binding reagent, B1

(ethanol); and in examples 5, 6, 7 and 8, single stranded nucleic acid was contacted with binding reagent B4 (70% ethanol in water).

Examples 9 and 10 of the Bastian et al. specification describe the selective binding of double stranded nucleic acid to a solid support without a binding reagent and examples 11 to 13 describe the separation of single stranded nucleic acid and double stranded nucleic acid from the same cell lysate. Specifically, in example 11, double stranded nucleic acid was first bound to a solid support in the presence of lysis buffer, L8, and the remaining single stranded nucleic acid was bound to a solid support in the presence of binding reagent B4 (70% ethanol in water). In example 12, single stranded nucleic acid was first bound to a solid support in the presence of binding reagent B4 (70% ethanol in water) and the remaining double stranded nucleic acid was bound to a solid support in the presence of binding reagents B1 (ethanol) and B5 (5.9 M GTC). Finally, in example 13, both single stranded nucleic acid and double stranded nucleic acid were bound to a solid support in the presence of binding reagent B1 (ethanol) and the double stranded nucleic acid was eluted from the support with washing buffer W5 (0.5 M GTC, 25 mM TRIS/HCl, pH 7.5, 10% ethanol) while the single stranded fraction remained bound.

Thus, all of the teachings in the Bastian et al. patent are directed to methods of separating single stranded nucleic acid from double stranded nucleic acid by contacting the single stranded nucleic acid with a material containing alcohol groups and there is no enabling support in the Bastian et al. patent for a method of separating single stranded nucleic acid from double stranded nucleic acid by contacting single stranded nucleic acid with a binding reagent consisting essentially of a chaotropic agent, a chelating agent and/or divalent positive ions as claimed in the present invention.

The language of the allowed claims of the Bastian et al. patent further supports applicants' position in this regard. In particular, claim 1, the broadest and only

independent claim of the Bastian et al. patent, recites a process for the separation of single-stranded nucleic acid from double-stranded nucleic acids by treatment of a biological source, thereof, said treatment comprising the steps of:

a) applying to a first mineral support an aqueous solution containing a sample of said source under conditions whereby said first mineral support adsorbs only one of said single- or double-stranded nucleic acids followed by, optionally, washing said first mineral support; and

b) applying to a second mineral support the other of said single-or double-stranded nucleic acids, which was not adsorbed by the first mineral support, in an aqueous solution containing materials with alcohol groups. (Emphasis added).

Thus, the invention described in the Bastian et al. patent, as represented by the claims of that patent, sets forth the requirement that the reagents used to separate single stranded nucleic acid from double stranded nucleic acid present in a mixture of the two nucleic acid types include materials that contain alcohol groups. There is no enabling disclosure anywhere in the Bastian et al. patent of a method of separating single stranded nucleic acid from double stranded nucleic acid by using reagents consisting essentially of materials as claimed in the present invention to bind single stranded nucleic acid to a solid support.

Claim 16 is amended herein to recite a method for separating single stranded nucleic acid from double stranded nucleic acid, comprising the steps of: contacting a mixture comprising both single stranded nucleic acid and double stranded nucleic acid with a first liquid comprising a chaotropic agent and a nucleic acid binding solid phase, wherein the first liquid has a composition such that the double stranded nucleic acid binds to the solid phase; separating the solid phase from a supernatant containing the single stranded nucleic acid; and contacting the supernatant with-a second nucleic acid binding solid phase and a second liquid consisting essentially of a liquid selected from the group consisting of:

a) a chaotropic agent;

b) a chaotropic agent and a chelating agent;

c) a chaotropic agent and divalent positive ions; and

d) a chaotropic agent, a chelating agent and divalent positive ions,

wherein the second liquid has a composition such that the resulting mixture of supernatant and second liquid allows for binding of the single stranded nucleic acid to the second solid phase.

Support for these amendments can be found in the language of the original claims and in the teachings of the specification. Specifically, the recitation in claim 16 that the single stranded nucleic acids in the supernatant are contacted with a second liquid consisting essentially of a chaotropic agent, a chelating agent and/or divalent positive ions is supported in the teachings throughout the instant specification and at least on page 7, lines 25-30 and in the language of the original claims.

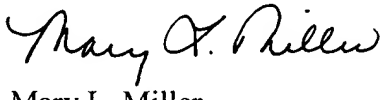
Claims 21, 39, 40 and 41 are amended herein for clarity and or to correct dependencies that changed due to cancellation of claims. Support for these amendments is found in the language of the original claims.

Thus, applicants believe that the claims as amended herein are adequately supported by the instant specification and respectfully request entry of these amended claims into the present application. On the basis of applicants' comments above regarding the absence in the Bastian et al. patent of any supporting disclosure of a method of isolating single stranded nucleic acid and double stranded nucleic acid in a mixture by using a second liquid consisting essentially of the materials as recited in the claimed invention, it is believed that the claims as amended are free from the cited art. Thus, applicants respectfully request the withdrawal of this rejection and allowance of the pending claims to issue.

Applicants request the opportunity to discuss this application with Examiner Tung and her Supervisory Examiner Gary Benzion before any further official actions are issued for this application. Applicants further request that any such further actions be reviewed and co-signed by Supervisory Examiner Benzion.

A check in the amount of $110.00 is included herewith as the fee for a one-month extension of time. This amount is believed to be correct. However, the Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

Respectfully submitted,



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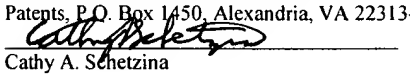

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